

Applicants: Tuschl et al.  
Serial No.: 10/589,449  
Filed: April 27, 2007  
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### **Preliminary Amendment**

Prior to the examination of the above-identified application, please amend the application as follows:

#### **IN THE CLAIMS:**

*This listing of claims will replace all prior versions and listings of claims in the application:*

1. (Withdrawn) An isolated single stranded anti-microRNA molecule comprising a minimum of ten moieties and a maximum of fifty moieties on a molecular backbone, the molecular backbone comprising backbone units, each moiety comprising a base bonded to a backbone unit, each base forming a Watson-Crick base pair with a complementary base wherein:

at least ten contiguous bases have the same sequence as a sequence of bases in any one of the anti-microRNA molecules shown in Tables 1-4, except that up to thirty percent of the bases pairs may be wobble base pairs, and up to 10% of the contiguous bases may be additions, deletions, mismatches, or combinations thereof;

no more than fifty percent of the contiguous moieties contain deoxyribonucleotide backbone units;

the moiety in the molecule at the position corresponding to position 11 of the microRNA is non-complementary; and

the molecule is capable of inhibiting microRNP activity.

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2. (Withdrawn) A molecule according to claim 1, wherein up to 5% of the contiguous moieties are additions, deletions, mismatches, or combinations thereof.
3. (Withdrawn) A molecule according to claim 1, wherein at least one of the moieties is a deoxyribonucleotide.
4. (Withdrawn) A molecule according to claim 3, wherein the deoxyribonucleotide is a modified deoxyribonucleotide moiety.
5. (Withdrawn) A molecule according to claim 4, wherein the modified deoxyribonucleotide is a phosphorothioate deoxyribonucleotide moiety.
6. (Withdrawn) A molecule according to claim 4, wherein the modified deoxyribonucleotide is N'3-N'5 phosphoroamidate deoxyribonucleotide moiety.
7. (Withdrawn) A molecule according to claim 1, wherein at least one of the moieties is a ribonucleotide moiety.
8. (Withdrawn) A molecule according to claim 7, wherein at least one of the moieties is a modified ribonucleotide moiety.
9. (Withdrawn) A molecule according to claim 8, wherein the modified ribonucleotide is substituted at the 2' position.
10. (Withdrawn) A molecule according to claim 9, wherein the substituent at the 2' position is a C<sub>1</sub> to C<sub>4</sub> alkyl group.
11. (Withdrawn) A molecule according to claim 10, wherein the alkyl group is methyl.

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12. (Withdrawn) A molecule according to claim 10, wherein the alkyl group is allyl.
13. (Withdrawn) A molecule according to claim 9, wherein the substituent at the 2' position is a C<sub>1</sub> to C<sub>4</sub> alkoxy - C<sub>1</sub> to C<sub>4</sub> alkyl group.
14. (Withdrawn) A molecule according to claim 13, wherein the C<sub>1</sub> to C<sub>4</sub> alkoxy - C<sub>1</sub> to C<sub>4</sub> alkyl group is methoxyethyl.
15. (Withdrawn) A molecule according to claim 8, wherein the modified ribonucleotide has a methylene bridge between the 2'-oxygen atom and the 4'-carbon atom.
16. (Withdrawn) A molecule according to claim 1, wherein at least one of the moieties is a peptide nucleic acid moiety.
17. (Withdrawn) A molecule according to claim 1, wherein at least one of the moieties is a 2'-fluororibonucleotide moiety.
18. (Withdrawn) A molecule according to claim 1, wherein at least one of the moieties is a morpholino phosphoroamidate nucleotide moiety.
19. (Withdrawn) A molecule according to claim 1, wherein at least one of the moieties is a tricyclo nucleotide moiety.
20. (Withdrawn) A molecule according to claim 1, wherein at least one of the moieties is a cyclohexene nucleotide moiety.
21. (Withdrawn) A molecule according to claim 1, wherein the molecule comprises at least one modified moiety for increased nuclease resistance.

22. (Withdrawn) A molecule according to claim 21, wherein the nuclease is an exonuclease.
23. (Withdrawn) A molecule according to claim 22, wherein the molecule comprises at least one modified moiety at the 5' end.
24. (Withdrawn) A molecule according to claim 22, wherein the molecule comprises at least two modified moieties at the 5' end.
25. (Withdrawn) A molecule according to claim 22, wherein the molecule comprises at least one modified moiety at the 3' end.
26. (Withdrawn) A molecule according to claim 22, wherein the molecule comprises at least two modified moieties at the 3' end.
27. (Withdrawn) A molecule according to claim 22, wherein the molecule comprises at least one modified moiety at the 5' end and at least one modified moiety at the 3' end.
28. (Withdrawn) A molecule according to claim 22, wherein the molecule comprises at least two modified moieties at the 5' end and at least two modified moieties at the 3' end.
29. (Withdrawn) A molecule according to claim 22, wherein the molecule comprises a nucleotide cap at the 5' end, the 3' end or both.
30. (Withdrawn) A molecule according to claim 22, wherein the molecule comprises an ethylene glycol compound and/or amino linkers at the 5' end, the 3' end, or both.
31. (Withdrawn) A molecule according to claim 1, wherein the nuclease is an endonuclease.

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32. (Withdrawn) A molecule according to claim 31, wherein the molecule comprises at least one modified moiety between the 5' and 3' end.

33. (Withdrawn) A molecule according to claim 31, wherein the molecule comprises an ethylene glycol compound and/or amino linker between the 5' end and 3' end.

34. (Withdrawn) A molecule according to claim 1, wherein all of the moieties are nuclease resistant.

35. (Currently Amended) A method for inhibiting microRNP activity in a cell, the microRNP comprising a microRNA molecule, the microRNA molecule comprising a ~~sequences~~ sequence of bases complementary ~~of to~~ to the sequence of bases in a single stranded anti-microRNA molecule, the method comprising introducing into the cell the single-stranded anti-microRNA molecule comprising a sequence of ~~a minimum of ten moieties~~ and a maximum of fifty moieties on a molecular backbone, the molecular backbone comprising backbone units, each moiety comprising a base bonded to a backbone unit, each base forming a Watson-Crick base pair with a complementary base, wherein:

~~at least ten contiguous bases of the anti-microRNA molecule are complementary to the microRNA, except that up to thirty percent of the bases may be substituted by wobble base pairs, and up to ten percent of the at least ten moieties are addition, deletions, mismatches, or combinations thereof;~~

~~no more than fifty percent of the contiguous moieties contain deoxyribonucleotide backbone units; and~~

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~~the moiety in the molecule at the position corresponding to position 11 of the microRNA is non-complementary, wherein said anti-microRNA molecule comprises the sequence of bases identified in SEQ ID NO: 445.~~

36. – 40. (Cancelled)

41. (Currently Amended) An isolated ~~microRNA~~ molecule comprising ~~a minimum of ten moieties and a maximum of fifty moieties on a molecular backbone, the molecular backbone comprising backbone units~~, wherein each moiety comprising comprises a base bonded to a backbone unit wherein:

~~at least ten contiguous bases have the same sequence as a sequence of bases in any one of the microRNA molecules shown in Table 2, except that up to thirty percent of the bases pairs may be wobble base pairs, and up to 10% of the contiguous bases are additions, deletions, mismatches, or combinations thereof, and~~

~~no more than fifty percent of the contiguous moieties contain deoxyribonucleotide backbone units~~ said molecule comprising the microRNA molecule identified in SEQ ID NO: 139 or its corresponding anti-micro RNA molecule identified in SEQ ID NO: 445.

42. (Cancelled)

43. (Original) A molecule according to claim 41, wherein the molecule is modified for increased nuclease resistance.

44. – 47. (Cancelled)

48. (Withdrawn) An isolated single stranded anti-microRNA molecule comprising a minimum of ten moieties and a maximum of fifty moieties on a molecular backbone, the

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molecular backbone comprising backbone units, each moiety comprising a base bonded to a backbone unit, each base forming a Watson-Crick base pair with a complementary base wherein:

at least ten contiguous bases have the same sequence as a sequence of bases in any one of the anti-microRNA molecules shown in Tables 1-4, except that up to thirty percent of the bases pairs may be wobble base pairs, and up to 10% of the contiguous bases may be additions, deletions, mismatches, or combinations thereof;

no more than fifty percent of the contiguous moieties contain deoxyribonuleotide backbone units; and

the molecule is capable of inhibiting microRNP activity.

49. (Cancelled)